capital sum such as he could never have saved during a lifetime of unremitting labour. The employer or his representative, the insurance company, is fair game. To question the moral issues of the situation would seem hardly more relevant to the claimant than to argue the ethics of unearned income, capital appreciation, or the take-over bid—phenomena which manifest the operation of similar motives at other levels of what he accepts without question as a ruthlessly acquisitive society.

How far has the socialization of large sectors of our economy influenced this situation and these attitudes? It can be said with some confidence, for example, that nationalization of the industry has radically affected the orientation of the coal-miner to his employing organization. The hatred of the miner for the coal-owner had its roots deep in history, and was felt with a passion unknown in other fields of industry. The miner of to-day grumbles with his fellows about bureaucracy, but he will defend the Coal Board vehemently against outside criticism. I think it would be an exaggeration to claim that he feels a close sense of identification with it. The chain of command is still too indirect for such identification to permeate the lowest levels of the industry. Nevertheless, the miner of to-day feels that in general the Board's interests are his own and that in the last resort their collaboration is vital to the survival of the industry and of the curiously individual pattern of society which it sustains.

The conception of accident neurosis outlined in these lectures would be strengthened if it were possible to claim that the incidence of the condition had been reduced by this change of ownership and attitude in the coal industry. No figures are available in this connexion, but the attitudes of the injured miner in the matter of claims for compensation do not appear to differ in any obvious way from those of workers employed by the larger private firms. Like other nationalized industries the Coal Board runs its own insurance scheme, generously administered and continuing a long tradition of settling nearly every case round the conference table. It is my impression that this scheme works better than where the responsibility has been handed over to an insurance company. Within the limitations of the industry, management makes great efforts to furnish light employment as soon as practicable, medical referees are often asked to adjudicate on conflicting medical reports, and the inevitable delays of litigation are avoided. But the successful operation of the scheme owes more to the responsibility of the men's representatives than to that of the claimants themselves. The best of these are men of the highest calibre and integrity who have spent a lifetime in the industry and who have too great a sense of social responsibility to have any patience with dishonesty or exaggeration.

If such information were available a third lecture could be written on the epidemiology of accident neurosis and its differential incidence in countries with different forms of political, judicial, and administrative organization. Personal experience suggests, for example, that it is probably a less conspicuous and ubiquitous problem in Eastern than in Western Europe. But he would be a bold man who ascribed any such apparent reduction in incidence to a change in ethos, rather than to the deliberate formulation of administrative policies which have rendered the disorder unprofitable and therefore without purpose.

I thank the patients, solicitors, and insurance companies who so generously gave of their time and trouble to ensure the completion of the clinical data; and my friends of the Bench and the Bar who have—I hope—purged my contribution of legal solecisms.

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A STUDY OF THE ANDROGENIC AND SOME RELATED EFFECTS OF METHANDIENONE

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Testosterone derivatives, apart from their virilizing action, may have, to a varying extent, any of the following effects (Dorfman and Shipley, 1956). (1) They may be anabolic, promoting nitrogen retention (in the form of protein) and muscle and organ growth. (2) They may depress other endocrine glands, and, for example, interfere with the oestrous cycle in women and depress spermatogenesis in men. (3) They may have a progestational effect. (4) They may cause salt and water retention. (5) They may inhibit the growth of cancer of the breast in females, and may increase the rate of growth of cancer of the prostate. (6) Some of the synthetic analogues of testosterone—namely, those with an alkyl group in the 17α position—may adversely affect liver function (Foss and Simpson, 1959; Wynn *et al.*, 1961).

The anabolic effect of the derivatives of testosterone may be of considerable clinical value in the treatment of certain wasting illnesses and senile and post-menopausal osteoporosis. They have also been used to counter the catabolic effects of long-term corticosteroid therapy. A most important application is in the treatment of breast cancer. In most of the conditions mentioned prolonged treatment with these steroids is required. It is therefore an advantage if the drug can be given by mouth rather than by injection. Unless the drugs are to be used for the treatment of

hypogonadism in males, there is also an advantage in using a compound which retains the anabolic effects of testosterone but has minimal virilizing action. Such a compound is methandienone.

Methandienone (1-dehydro-17α-methyltestosterone; "dianabol") is very similar in structure to methyltestosterone, differing only in the presence of a double bond between carbon 1 and 2 in the A ring of the steroid nucleus. It is active when given by mouth. Desaulles *et al.* (1959) found that in the rat it was as powerful an anabolic steroid as testosterone propionate or methyltestosterone, but had little of the androgenic action of these latter two steroids.

We have studied the metabolic effects of methandienone, and have found that it has a powerful anabolic action. We hope to report these studies separately. It

TABLE I.—*Clinical Details of Seven Pre-menopausal Women Given Methandienone*

Case No.	Age	Diagnosis	Dose and Duration of Methandienone Therapy (mg./Day)	Acne	Hair			Voice	Libido	Musculature	Defeminization	Ext. Genitalia	Sense of Well-Being	Effect on Menses
					Scalp	Face	Body							
4	37	Renal tubular acidosis with nephrocalcinosis	25 for 200 days*	−	−	−	−	−	−	−	−	−	−	Regular periods till start of methandienone. None since being on drug
7	28	Severe Raynaud's disease	20 for 210 days*	−	−	−	−	−	++	−	−	−	−	Regular periods till start of methandienone. One short period after 20 days on drug. None since
13	26	Septic abortion. Acute tubular necrosis. Cachexia	25 for 22 days	++	−	−	−	−	−	−	−	−	+	No periods since septic abortion two months prior to methandienone therapy
29	39	Anorexia nervosa	20 for 16 days	−	−	−	−	−	+	−	−	−	−	No periods for 18 months prior to methandienone. First normal period after 10 days on drug
30	26	,, ,,	20 for 10 days, then 15 for 10 days, 10 for 8 days, and 5 for 6 days	−	−	−	−	−	−	+	−	−	−	No periods for 5 years prior to methandienone therapy
31	44	Severe asthma on triamcinolone	50 for 14 days, then 25 for 82 days*	+	−	+	−	−	−	−	−	−	+	Regular periods till start of methandienone, one normal period after 8 days on drug. None since
32	52	Chronic bronchitis and asthma on triamcinolone	25 for 100 days*	++	−	−	−	−	−	+	−	−	+	Regular periods till start of methandienone. None since being on drug

* Still on methandrienone at time of completing present study.

TABLE II.—*Clinical Details of 12 Post-menopausal Women Given Methandienone*

Case No.	Age	Diagnosis	Dose and Duration of Methandienone Therapy (mg./day)	Acne	Sebaceous Secretion	Hair			Voice	Libido	Musculature	Defeminization	Ext. Genitalia	Sense of Well-being	Effect on Menopausal Symptoms, if Present
						Scalp	Face	Body							
1	60	Acute intermittent porphyria. Postmenopausal osteoporosis	50 for 33 days, then 25 for 160 days*	−	−	−	−	−	−	−	−	−	−	++	None present
3	50	Acute glomerulonephritis. Cachexia	25 for 70 days	−	−	−	−	−	±	++	++	+	−	++	Severe menopausal symptoms completely stopped while on methandienone
5	28	Cushing's syndrome. Peptic ulceration	50 for 27 days, then 100 for 12 days. 50 for 12 days, 12·5 for 29 days, and 30 for 130 days	++	−	−	±	−	−	−	+	−	−	++	Mild menopausal symptoms stopped while on methandienone
6	60	Systemic lupus erythematosis on prednisone. K^+-losing pyelonephritis. Cachexia	50 for 40 days, then 12·5 for 80 days, and 25 for 40 days	−	−	−	−	−	−	−	++	+	−	+	None present
9	43	Severe pyelonephritis. Anorexia nervosa	25 for 260 days*	−	−	−	−	−	−	−	−	−	−	+	,, ,,
10	75	Post-gastrectomy diarrhoea. Malnutrition	25 for 33 days and 201 days*	−	−	−	−	−	−	−	++	−	−	++	,, ,,
11	51	Chronic pyelonephritis. Malnutrition	50 for 7 days, then 25 for 44 days	+	+	−	−	−	−	−	+	+	−	+	Moderate menopausal symptoms stopped while on methandienone
15	62	Carcinoma of breast with bone and liver metastases	25 for 10 days	−	−	−	−	−	−	−	−	−	−	−	None present
16	37	Cushing's syndrome. Carcinoma of adrenal cortex with liver metastases	50 for 10 days	−	−	±	±	−	−	−	−	−	−	−	,, ,,
17	47	Chronic bronchitis and asthma on prednisone	50 for 43 days, then 25 for 60 days*	+	−	−	−	−	−	−	+	−	−	++	Mild menopausal symptoms stopped while on methandienone
19	83	Ischaemic peripheral arterial disease. Malnutrition	50 for 41 days	−	−	−	−	−	−	−	+	−	−	++	None present
26	52	Post-gastrectomy abdominal fistula. Cachexia	50 for 96 days	+	+	+	−	+	+	−	++	+	−	++	,, ,,

* Still on methandienone at time of completing present study.

was considered important to verify the dissociation of the anabolic from the androgenic effects of methandienone in man. We report here our experiences of (*a*) the androgenic effect of methandienone, (*b*) the effect of methandienone on menstruation, (*c*) the effect of methandienone on menopausal symptoms, and (*d*) the psychological effects of methandienone.

Case Material.—We have divided the patients into three groups—namely, pre-menopausal women (7 cases), post-menopausal women (12 cases), and adult males (11 cases). The clinical details of these cases are summarized in Tables I, II, and III.

Androgenic Effect of Methandienone

The following possible evidence of an androgenic action was looked for in the female patients: acne and increased sebaceous secretion of the face and scalp, tendency to loss or thinning of scalp hair, increase in facial or body hair, increase in musculature, increase in libido, changes in the pitch of the voice, and changes in the external genitalia or evidence of defeminization.

It is recognized that some of these changes—for example, increase in musculature and in libido—would be at least partly attributable to the anabolic action of the drug, as opposed to a specific virilizing action.

Acne and Increase in Sebaceous Secretion

Severe acne was not a common complication of treatment with methandienone. Of the 12 post-menopausal women, four developed acne. In Case 11 there was a mild acneiform eruption around the mouth, chin, and forehead after 40 days on methandienone (25 mg. a day). In this patient there was also an increase in greasiness of the scalp and face. In Case 26 50 mg. of methandienone a day was given for 96 days; there was a similar acneiform eruption on the face, also associated with increased sebaceous secretion, after the patient had been on 50 mg. of methandienone for a continuous period of 70 days. In Case 5, a patient suffering from Cushing's syndrome with mild virilizing symptoms (loss of scalp hair, increased facial hair), a very marked acneiform rash involving the whole of the back developed after she had been on a very prolonged course of methandienone. At the time the rash developed the patient was receiving only 12.5 mg. of methandienone a day. Subsequently this dose was increased to 30 mg. and continued for another 130 days. Despite this increase in dosage the acne responded rapidly to local treatment with resorcin and sulphur, and it did not recur subsequently. In Case 17 there was a minimal acneiform eruption of the back after 25 mg. of methandienone daily for 30 days. This has subsequently started to clear despite continuation of the drug.

Of the seven pre-menopausal women, three developed acne. In Case 13 this was an extremely pustular form of acne, involving the forehead, which came on suddenly after the patient had been receiving 25 mg. of the drug daily for 22 days. This patient had diminished renal function, and at the time of the appearance of the eruption was running a higher fever—101–103° F. (38.3–39.4° C.)—from a severe pelvic infection. Methandienone therapy was stopped and the rash cleared within 12 days, leaving minimal scarring. Cases 31 and 32, both on prolonged corticoid therapy for severe asthma, developed acne while on methandienone. This mainly involved the back, there being no visible eruption on the face.

Changes in Scalp Hair.—In the seven pre-menopausal women no change in scalp hair was noticed while on the drug. Of the twelve post-menopausal women only one (Case 26) complained of thinning of the scalp hair, with more coming away on the comb. This occurred after she had been having 50 mg. of methandienone daily for two months. Cases 5 and 16 already had marked thinning of the scalp hair due to Cushing's syndrome, and in Case 5 the hair actually became thicker and less fragile while on methandienone.

Increase in Facial or Body Hair.—In only three patients was any increase in facial hair noticeable. In two of these (Cases 5 and 16) facial hirsuties was already present due to Cushing's syndrome, and the slight increase noted cannot with certainty be attributed to methandienone. Similarly in Case 31 the patient had had facial hirsuties prior to starting the drug, probably associated with the high corticoid doses she was being given for severe asthma. Although she did not notice any increase in this hirsutism while on methandienone, it was apparent to the medical staff.

Increase in Musculature.—It is difficult to know how much reliance can be placed on this as a sign of virilization, as it is primarily a result of anabolism. Many cases exhibited some increase in muscle mass and in muscle power while on the drug. In the pre-menopausal group of women no case exhibited this to any marked extent. In the post-menopausal group it occurred in several cases, being most marked in Cases 3, 6, 10, and 26. Only in Case 3 was this of any embarrassment; the patient felt that it was making her rather male-like.

TABLE III.—*Clinical Details of* 11 *Male Patients on Methandienone*

Case No.	Age	Diagnosis	Dose and Duration of Methandienone Therapy (mg./day)	Acne	Sebaceous Secretion	Hair			Libido	Musculature	Sense of Well-being
						Scalp	Face	Body			
2	28	Acute idiopathic osteoporosis	100 for 26 days, then 75 for 198 days	+	+	±	−	−	+	+	++
8	53	Pancreatic steatorrhoea malnutrition	50 for 65 days*	−	−	−	−	−	−	+	++
12	21	Idiopathic hypercalciuria	50 ,, 14 days	−	−	−	−	−	++	−	−
18	24	,, ,,	50 ,, 10 ,,	−	−	−	−	−	+	−	−
20	70	Prostatic enlargement. Pyelonephritis. Cachexia	100 for 6 days, then 50 for 19 days	−	−	−	−	−	−	+	++
22	28	Addison's disease	25 for 8 days, then 8 days off and then 25 mg. for 8 days	−	−	−	−	−	−	−	−
23	30	Idiopathic steatorrhoea. Malnutrition	50 for 98 days*	−	−	−	−	−	−	++	++
24	21	Cushing's syndrome	100 for 22 days	−	−	+	−	−	−	+	+
25	30	Perforated peptic ulcer. Peritonitis. Intestinal fistula. Cachexia	100 for 11 days, then 50 for 15 days, and 25 for 7 days	−	−	+	−	−	−	+	++
27	16	Chronic pyelonephritis with renal failure	100 for 2 days, then 50 for 32 days	−	−	−	−	−	−	−	+
28	14	Anorexia nervosa	10 for 8 days, then 15 for 12 days, and 20 for 6 days	−	−	−	−	−	−	−	−

* Still on methandienone at time of completing present study.

Increase in Libido.—Increase in libido was a prominent symptom of methandienone therapy in two cases. It occurred quite early on in the course of the treatment, within the first week. It occurred in one of the seven pre-menopausal women (Case 7) and in one of the 12 post-menopausal women (Case 3). In Case 7 the effect on libido decreased after about four weeks and was absent after about eight weeks.

Increased libido would seem to indicate some androgenic property of methandienone. However, the control of libido is a complex subject, dependent as it is on psychological and other factors, apart from the androgens. It could in part be explained by the sense of well-being which the drug imparts and the anabolic action of the drug. The increase in libido did not occur in patients over 50.

Change in Pitch of Voice.—Deepening or huskiness of the voice would be expected in those women on a long course of methandienone if the drug had any marked androgenic properties. In fact, in no case did any change in the voice occur, with the possible exception of Case 3, who at times had slight huskiness. Both she and her husband, however, thought that this had been present for many years and was not influenced by the drug.

Evidence of Defeminization, or Change in External Genitalia.—Four patients (Cases 3, 6, 11, and 26) had a facial appearance that was rather more masculine while on the drug. This is difficult to describe, but consisted of increased prominence of the facial bones, loss of the smooth facial contours, and a tendency for increased plethora of the cheeks. Only in Case 3, combined with her increased musculature, did the patient comment on this defeminization. In no case was it so obvious as to be noticed by husband or friends. In none of the patients was there any noticeable atrophy of breast tissue or loss of female body configuration. Changes in the external genitalia were not directly looked for in the female patients. None of the female patients themselves, however, noticed any changes in their external genitalia when they were questioned about this.

Effect of Methandienone on Male Patients

No drug can be said to be virilizing in respect of a male after puberty unless the male has absence of normal testicular function. It is thus difficult to label certain of the actions of methandienone in men.

Of the 11 male patients, only one (Case 2) developed acne and increased sebaceous secretion. In this patient it did not occur until after 200 days of continuous treatment with a very high dosage of the drug (75–100 mg. daily). The acne was of minimal degree, involving the back and shoulders. It was not pustular and did not necessitate treatment.

Only three men (Cases 2, 24, and 25) considered that there might have been thinning of the scalp hair while on the drug. Case 2 had, however, had this thinning of the scalp hair prior to starting methandienone, and he was not certain whether the drug had caused it to increase in extent and severity. The other two patients (Cases 24 and 25) were quite certain that methandienone had caused thinning of the scalp hair, although clinically this was not obvious.

None of the male patients noticed any change in the amount or texture of their facial or body hair while on the drug, and none had to shave more frequently.

Three men noticed an increase in libido while on methandienone (Cases 2, 12, and 18), consisting in increased sex awareness and increase in the frequency of erections and nocturnal emissions. In addition, the patient with Cushing's syndrome (Case 24) commented that his libido had returned to its pre-disease level while on methandienone.

Prostatic hypertrophy is usually a contraindication to the giving of testosterone derivatives, as the androgens act preferentially to cause further prostatomegaly, with the risk of acute urinary retention. It is therefore of interest that Case 20, a patient suffering from prostatomegaly, had no increase in prostatic symptoms although he was given 100 mg. of methandienone daily for six days, followed by 50 mg. daily for 19 days. He was admitted to hospital with a ruptured appendix, after which he had peritonitis and paralytic ileus. He ran a prolonged fever and became greatly wasted. The improvement in his general condition produced by the drug enabled a prostatectomy to be carried out with safety.

Effect of Methandienone on Menstruation

Of the seven pre-menopausal patients, two (Cases 13 and 30) were not having periods at the time of starting methandienone. One (Case 13) had had no periods since a septic abortion two months prior to her course of methandienone. Two months after stopping the drug her menstrual periods restarted and since then have been regular. The other (Case 30), with severe anorexia nervosa, had had amenorrhoea for the five years prior to admission to hospital. Her menses did not recommence during the giving of methandienone nor in the subsequent two months.

Case 29 also had anorexia nervosa, with gross wasting and amenorrhoea for the 18 months prior to her admission. In hospital on a high-protein, high-calorie diet, she rapidly gained weight and was in strong positive nitrogen balance. Menstruation recommenced 23 days after admission, despite her being given 20 mg. of methandienone daily for 10 days before her periods started.

The remaining four pre-menopausal patients (Cases 4, 7, 31, and 32) all had normal and regular menstrual periods prior to being started on methandienone. Cases 4 and 32 have had amenorrhoea since taking the drug (25 mg. daily for 200 and 100 days respectively).

Case 7 had one menstrual period of two days' duration with minimal loss after she had been on methandienone (20 mg. daily) for 20 days. In the subsequent 190 days of methandienone therapy she has had no further periods.

Case 31 had one normal period eight days after starting on triamcinolone (6 mg. daily) and methandienone (50 mg. daily). She has had no further menses in the subsequent 82 days of therapy, despite the dose of triamcinolone and methandienone being lowered to 2 mg. daily and 25 mg. daily respectively.

One of the post-menopausal women (Case 3) is of interest in the present connexion. This patient, aged 50, had had no periods for the two years prior to starting methandienone. During the last week of a 70-day course of the drug (25 mg. daily) there was slight loss of blood lasting two days. A dilatation and curettage at this time showed a smooth endometrial surface, and no scrapings could be obtained. The vaginal "spotting" had ceased before discontinuing methandienone. Ten

days after stopping the drug the patient had an apparently normal menstrual period, followed by a second period four weeks later. Since then there has been amenorrhoea.

None of the other post-menopausal women had any vaginal bleeding while on methandienone or after the drug was stopped.

Effect of Methandienone on Menopausal Symptoms

Four of the 12 post-menopausal women in the present study were complaining, to a variable degree, of symptoms attributable to the menopause. In these patients, as well as in three others with menopausal symptoms who have been seen by us but who are not included in the present series, methandienone rapidly stopped these symptoms.

During the two years when Case 3 had no periods she had been having frequent episodes of flushing and perspiring three or four times daily, each episode lasting about five minutes. At times she also felt rather depressed and had occipital "tension headaches." After the first three days on methandienone therapy the episodes of flushing and perspiring stopped, and did not recur during the 70 days on which the drug was given. As mentioned in the previous section, this patient had slight vaginal "spotting" during the final week of methandienone administration, a diagnostic dilatation and curettage at that time showing a smooth endometrial surface. In the 10 weeks after stopping the drug she had two apparently normal periods. It was only after this that her menopausal symptoms returned; these have persisted ever since, associated with amenorrhoea.

Case 5 had had occasional flushing for two years prior to admission. These stopped after the second week of methandienone and did not recur during the 210 days the drug was given. They began again, however, five days after stopping the drug.

Cases 11 and 17 had had moderate and mild menopausal symptoms respectively in the two years prior to admission. These consisted of flushing, redness and perspiration, and occipital headaches. These symptoms stopped when methandienone was given.

Apart from the slight bleeding seen in Case 3, no other post-menopausal patients had vaginal bleeding while on methandienone or immediately after stopping the drug.

Psychological Effects of Methandienone

An increased feeling of confidence with a sense of well-being was one of the most prominent changes that occurred in several of the patients while on methandienone. It was often remarked on, not only by the patients but by the nursing staff.

The psychological effects consisted of a brighter mental outlook, of a feeling that they could cope with their disease, and of feeling stronger and more confident; they were also associated with an increased appetite. This feeling of well-being was especially notable and of the greatest therapeutic value in the elderly patients with chronic illness—in such patients the results with methandienone were best summed up by the ward sister's remark, "They feel that they can deal with their illnesses as they would have done when they were young and healthy."

Methandienone had no psychological effects on those patients whose illnesses did not produce symptoms of ill-health. For example, it had no effect psychologically on three patients (Cases 4, 12, and 18) to whom methandienone was given to lower the urinary calcium. Three patients with anorexia nervosa (Cases 28, 29, and 30) on a high-calorie high-protein diet were in positive nitrogen balance, were gaining weight, and felt well at the time methandienone was started, and in these three cases it also had no psychological effects. Case 7, apart from her severe Raynaud's disease, felt well at the time of being given the drug, and again no psychological effects resulted.

Three patients who were chronically ill derived no psychological benefit from methandienone. In Case 22, with Addison's disease, the drug produced neither a physical nor a psychological effect. The other two (Cases 15 and 16) who showed no improvement in outlook or well-being suffered from carcinoma with multiple secondaries and had only a relatively short course of methandienone (25 and 50 mg. daily for 10 days respectively). It is of interest that, despite the absence of mental improvement, the drug induced a strong anabolic phase in both, as evidenced by their nitrogen balance.

An increased sense of well-being occurred in 19 of the 30 patients in the present study, usually within the first week of methandienone therapy. Among the seven pre-menopausal women it was a feature in Cases 13, 31, and 32, the latter two of whom had severe asthma and were on long-term corticoid therapy.

An increased sense of well-being occurred in 10 of the 12 post-menopausal patients. In particular it was the older patient who found the greatest psychological benefit from the drug. Two patients, aged 75 and 83 (Cases 10 and 19), rapidly felt much better once on methandienone.

Of the male patients it was again the older patients or the more severely ill in whom the psychological benefit of methandienone was most obvious. Case 20, aged 70, made a rapid physical and mental improvement while on the drug; while Case 8, who prior to methandienone was quite exceptionally uncooperative, unhelpful, and also depressed, once on the drug underwent a marked personality change, felt that he was going to get better, and became reasonably pleasant and easy to nurse.

Discussion

It is likely that any anabolic steroid that is a derivative of testosterone will have some androgenic effect if it is given in a high dosage for a prolonged period.

In rats methandienone has an anabolic effect as great as or greater than other anabolic steroids, such as testosterone propionate, methyltestosterone, norethandrolone, and norandrostenolone phenylpropionate (Desaulles *et al.*, 1959). In nitrogen balances carried out on 16 patients in the present study we found methandienone to have a powerful anabolic effect.

In studies on the castrated rat, Desaulles *et al.* (1959) found it to have approximately one-hundredth the androgenic effect of testosterone propionate, and one-seventeenth the androgenic effect of norethandrolone. With the capon-comb test its androgenic effect was even less.

Foss (1960) found no evidence of androgenic activity of the drug in four women, even when doses of up to 1.6 mg./kg./day were employed for periods of up to 29 weeks. With doses in excess of 0.5 mg./kg./day in children, however, some evidence of androgenic effects was observed.

In the present study methandienone did not appear to have any marked virilizing side-effects, if one excludes those patients who had high levels of endogenous or exogenous corticoids. Acne, increased sebaceous secretion, and changes in facial, body, and scalp hair were uncommon, while voice changes have not occurred. In the two women with Cushing's syndrome, however, and in four patients receiving either prednisone or triamcinolone, methandienone did produce some androgenic effects, though these were never of a very severe degree, and did not necessitate the discontinuation of the drug. The increase in libido that occurred in some patients is of interest, and may indicate some androgenic action.

The relative lack of androgenic effect of methandienone in this series is particularly relevant in that initially we were uncertain of the dosage necessary to produce anabolism, and consequently in the early periods of our study we used an excessively high dose. From our present studies of nitrogen balance, doses of 0.2–0.4 mg./kg. body weight per day are capable of producing marked nitrogen retention and gain in weight. Initially many of the patients were given methandienone in doses in excess of 1 mg./kg. body weight per day.

In the rat, Desaulles *et al.* (1959) found that inhibition of oestrus could be brought about only by high doses of methandienone (30 mg./day)—methyltestosterone and norethandrolone being 30 times more active inhibitors of the oestrous cycle. They also found methandienone to have a very weak progestational effect, large doses (70 mg./kg.) being unable to produce a complete progestational type of secretory epithelium in castrated female rabbits sensitized with oestrone.

Foss (1960) found no suppression of the menses in two women given 25 mg. and 50 mg. of methandienone daily, though the drug caused suppression of the menses in one 14-year-old girl. In the small number of pre-menopausal patients in the present series who had normal and regular periods prior to starting methandienone, the drug has completely suppressed menstruation. The suppression of menstruation in these patients had persisted for from 100 to 200 days at the time of reporting this study. The suppression of menstruation and of menopausal symptoms is probably due to methandienone inhibiting the function of the pituitary gland.

Methandienone appeared to have no progestational effect. It caused no rise of body temperature, nor was there any withdrawal bleeding.

The increased sense of well-being found in many patients while on methandienone was of considerable therapeutic value. It did not occur in patients who were not symptomatically ill at the time of being given the drug, but was most pronounced in the older or chronically ill patient.

This sense of well-being may be attributable to the anabolic or possibly some other action of methandienone, rather than to any androgenic property. These changes were not similar to the euphoria seen in some patients on cortisone or in some patients with disseminated sclerosis or general paresis of the insane. It did not consist of unjustified cheerfulness, but occurred at a time of positive nitrogen balance, weight gain, and symptomatic improvement. It did not cause the undesirable psychological manifestations often seen with cortisone, such as nervousness, restlessness, and insomnia, nor did it ever produce a psychotic state.

Summary

During the past two years the effects of methandienone have been studied. Androgenic effects were slight or absent when a dose of the drug capable of producing marked anabolism was given, and, in several cases, even when the dose used was greater than that required to produce the maximum therapeutic effect.

Methandienone may suppress menstruation and menopausal symptoms when these are present.

In many patients, especially in the old or chronically ill, methandienone produced a sense of well-being and increased confidence. Unlike the effects of corticoid or corticotrophin administration, restlessness, nervousness, or insomnia did not occur.

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PREGNANCY IN AN ADRENAL PSEUDOHERMAPHRODITE TREATED WITH CORTISONE

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Congenital adrenal virilism is caused by an inborn error of metabolism in which an inherited enzyme defect is responsible for excessive production of androgens and a diminished secretion of other cortical hormones (Jailer, 1953 ; Mason and Morris, 1953). The beneficial effects of cortisone, or its synthetic analogues, were demonstrated first by Wilkins *et al.* (1952): androgen production drops to normal and feminine characters emerge.

An obvious criterion of success in long-term therapy is the maintenance of a normal pregnancy. This paper records successful pregnancy and the birth of a normal child to a patient whose congenital adrenal virilism was not treated until adult life.

Case History

The patient, born in 1928, was seen at the London Hospital in 1954 complaining of amenorrhoea and beard-growth. At the age of 4 years enlargement of the clitoris had been noted and pubic hair was present at the age of 7. By the age of 11 she had a considerable amount of body hair, and facial hair growth had just begun. Subsequently this became so marked that daily shaving was required. Throughout childhood she grew faster than her contemporaries but stopped growing in her thirteenth year. From infancy until her fourteenth year she had suffered from episodic attacks of severe vomiting which prostrated her for two or three days. These attacks were usually precipitated by minor infections but became less severe and less frequent as she grew up. She had never menstruated.

Family History.—Four sisters were normal, but the fifth was suspected of having a genital abnormality. This girl (aged 8 years) was examined in 1954 and found to be an adrenal pseudohermaphrodite with virilism and a high 17-ketosteroid excretion. Treatment with cortisone diminished the virilism and in due course she went through a normal female puberty and achieved a regular menstrual cycle.